caeruleus. Alterations such as nerve cell loss and atrophy, presence of Lewy bodies, and neurofibrillary tangles within nerve cells occurred to a significant extent in cases of dementia pugilistica in retired professional boxers, Parkinson's disease, Jakob-Creutzfeldt disease, and progressive supranuclear palsy; but they were minimal in normally aged control individuals (age range 30-97 years) and in those with motor neurone disease. Protein-synthesising capability, as indicated by nucleolar volume,[3] was reduced significantly in remaining cells in cases of dementia pugilistica and Jakob-Creutzfeldt disease; but it was unaltered, even in the middle-aged and elderly controls, in motor neurone disease, and in the few remaining cells in cases of Parkinson's disease and progressive supranuclear palsy. A variable degree of mental impairment was common to all cases in this study where there was involvement of the locus caeruleus, ranging from mild loss of intellectual powers and confusion in cases of Parkinson's disease to overt dementia in cases of dementia pugilistica and Jakob-Creutzfeldt disease—cases of progressive supranuclear palsy being intermediate in this respect. By contrast, the control group, which was specifically screened for loss of mental ability, and the cases in the motor neurone disease group were all mentally preserved.

Adrenergic pathways from the locus caeruleus and dorsal motor nucleus of the vagus nerve, in conjunction with afferents to these regions from the supraoptic and paraventricular nuclei of the hypothalamus, form a system which through its connections with the periphery maintains homoeostasis within the central nervous system against adverse extracerebral conditions.[4] These pathways seem to regulate the permeability of the brain's microcirculation to water and water-soluble metabolites.[4] It is, therefore, possible that the mental impairment or, more specifically, the dementia that is seen in Alzheimer's disease, and to varying extents in the other conditions we have outlined, is related to a breakdown in the functional integrity of this homoeostasis-maintaining system. Such an impairment would lead to disturbed transport between brain and circulation, with widespread consequences for the nerve cells' capability to produce the proteins for correct neurophysical function.[5]

However, that is not to say, nor is it implied, that the aetiology or indeed the pathogenic mechanisms behind the changes in the locus caeruleus are the same in all conditions where dementia is a feature; rather the dementia represents a common picture of physiological outcome stemming from basically unrelated pathological causes.

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Chlormethiazole and temazepam

SIR,—Dr R S Briggs and others (1 March, p 601), in a study of the pharmacokinetics and pharmacodynamics of chlormethiazole and temazepam following single oral night-time doses, reported that the mean elimination half life of temazepam was of the order of 14 hours in a group of 10 elderly subjects (mean age 72·9 years), although insufficient data were available to permit the calculation of individual half lives. The subjects were largely symptomless and did not receive concomitant drug therapy.

We have studied the pharmacokinetics of temazepam in a group of elderly hospital inpatients (four female, two male) (mean age 80±6 (SD) years) following a single 20 mg oral dose of temazepam (Euhypnos, Montedison). Venous blood (5 ml) was obtained at frequent intervals up to 56 hours after the dose, and plasma temazepam concentrations were measured by a modification of the method of Belvedere *et al.*[1] The mean of the individual elimination half lives was found to be 17·6±2·8 hours. None of the patients had acute hepatic, renal, or cardiac disease; three patients were receiving no drug therapy, two were prescribed diuretics for mild heart failure, and the remaining patient was under treatment with chlormethiazole (Heminevrin) and Distalgesic. In contrast, in an analogous study performed using healthy volunteers (four male, two female; mean age 29±5 years), the mean of the individual elimination half lives was 8·0±1·8 hours.

Dr A F Macklon and others (22 March, p 861) pointed out that the data of Dr Briggs and others could suggest a mean temazepam half life of up to 26 hours in the elderly subjects studied, and that accumulation of the drug on chronic daily dosage with the attendant possibility of adverse side effects was possible. Our results support this contention with respect to some elderly inpatients, since it is likely that accumulation will occur with daily dosage when the elimination half life exceeds 16 hours.[2] This is supported by the results of a further study, where we have observed a 1·5-fold increase in the temazepam plasma concentrations in early morning specimens after once-nightly dosage with temazepam (20 mg) for one week in elderly inpatients.

We are currently investigating the pharmacokinetics of the drug in healthy elderly subjects; but until this has been done the drug temazepam, like most other benzodiazepines, cannot be regarded as entirely safe or free from hangover effect in the elderly.

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Drugs and the elderly

SIR,—In the article "Drugs and the elderly" (10 January, p 125), by Drs Lawrence E Ramsay and Geoffrey T Tucker, though the authors accept that polypharmacy prevails in the elderly they state "What is not known is how much of prescribing is unnecessary, ineffective, or inappropriate. Indeed, we may never know. . . ." It is an everyday experience of a geriatrician to see at least half of the patients admitted taking eight to 10 kinds of tablets, more than half of these being far from essential. It has been shown that most elderly patients cannot take more than three concurrent regular medicines reliably[1] and patients who are prescribed several medicines or frequent doses are more likely to make mistakes.[2-3]

The problem of non-compliance, in the elderly at least, is too difficult to be overcome simply by giving written instructions, as suggested by authors. Poor eyesight contributes to many errors, especially so for those living alone; and small or indistinct writing makes some labels illegible even for those with good eyesight.[2-3] Training elderly patients, for two weeks before the date of foreseeable discharge, how and when to take their own medicine helped compliance.[4] Also a 15-minute instruction by a designated member of the staff to the patient before discharge from the hospital was shown to reduce the errors significantly even in the poorly orientated.[5] Further, I doubt whether a surprise raid on the home of an elderly person, as suggested by the authors, would make any difference to compliance—it would simply make the patient more apprehensive and less co-operative. Instead, a regular visit by a friendly district nurse ensures a regular intake of drugs even in the most difficult cases, as many geriatricians would agree.

Lastly, may I add that the number of people over the age of 65 in the United Kingdom is not 12% but more than 14% ?

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ABC of blood pressure reduction

SIR,—If hypertension improved survival, increased intellectual capacity, or ensured physical independence there would be queues at the surgeries to find out whether the individual had hypertension or not, and if not why not.

In fact, we know from the insurance companies[1] and from the epidemiological studies in communities like Framingham in the United States[2] that hypertension reduces survival, may cause the multi-infarct type of dementia, and as an accelerator of the arteriosclerotic process is associated with loss of independence and indeed severe and protracted morbidity associated with stroke disease. It has been said repeatedly that there is little evidence to justify treatment of the elderly with drugs to lower the blood pressure but, since most of the drug trials have been confined to patients below 65 years of age, neither is there good evidence that preventing hypertension, or reducing hypertension, in the older patient will do any harm. It is true that Jackson *et al*[3] described cases of stroke precipitated by treatment; this paper, however, is not a reason for discarding treatment of hypertension but is simply a warning of the consequences that accrue when potent drugs are used in excessive dosage when not warranted by the clinical condition. It is always easier not to treat, especially the "symptomless," but this does not mean that it is correct. The institution of treatment, however simple the schedule, lays on the prescribing doctor the onus of supervision to ensure that the desired effect is achieved, that therapy is being taken, and that no untoward reaction has occurred.

The need to consider treatment is now more relevant than ever before as treatment regimens have been simplified to improve compliance and it has been demonstrated that blood pressure can be reduced in the elderly with simple regimens and without serious side effects.[4] Since not only is hypertension a hypothetical risk factor in the causation of stroke[2] but it

has been shown that there is an increased prevalence of hypertension in the patients with established stroke disease,[5] the prospect that better management of blood pressure in the middle-aged and elderly patient will reduce frequency of stroke disease merits the very careful and meticulous examination that is being carried out by the European Working Party on Hypertension in the Elderly. (EWPHE). Nevertheless, this trial has already been in being for five years and may take several more years to reach completion; in the meantime the available treatment regimens have changed considerably and will merit further trials irrespective of the conclusions reached by the EWPHE.

Dr R D Kennedy (17 January, p 226) suggests that the matter should be taken to avizandum while we await the outcome of the European trial; but there are to my knowledge few trials being conducted to be taken to avizandum and, unless clinicians and practitioners are prepared to take a more active interest than this, the problem will remain unresolved and the advantages of improved therapeutic regimens unexplored.

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SIR,—May we revert to the question that we raised (13 December, p 1636) about whether oestrogens in the dosages commonly used at the menopause raise blood pressure? This is an important clinical problem at this age. The literature on the subject is scanty and conflicting.

Crane *et al*[1] reported a study of 20 hypertensive patients referred for investigation who were found to be taking conjugated oestrogen (Premarin, dosage unspecified). In five of these patients a record of normal blood pressure before they had started oestrogen therapy was found in the physician's notes, albeit up to five and six years previously. In these patients the blood pressure appeared to go down after stopping the oestrogen. What the blood pressure did in the other 15 is not recorded.

In 1976 Pfeffer *et al*[2] published a case-control study which examined hospital records and death registration in a retirement community from 1964 to 1973 to ascertain the prevalence of hypertension and oestrogen use in stroke patients. Two hundred and thirteen cases and 1065 controls were studied. Pretreatment blood pressure readings were recorded in 88% of users and in 56% of controls—that is, in only 783 patients out of 1278. A highly significant association was found between oestrogen use and hypertension. However, no attempt was made to measure blood pressure during therapy. The criteria for designating "hypertension" were as follows: (*a*) a past history of hypertension (apparently at any time); (*b*) current diagnosis of and therapy for hypertension, (*c*) two or more recorded levels of greater than 160 mm Hg (systolic) or 85 mm Hg (diastolic), phase unspecified. These criteria are so vague that the most likely reason for the association is that they were a group of women who were big users of therapy of all kinds, either ready acceptors or the patients of therapeutic enthusiasts.

Spellacy *et al*[3] measured serial blood pressure in women taking conjugated oestrogen, mestranol, and ethinyloestradiol; and they found a significant rise in blood pressure only in patients taking ethinyl oestradiol, 0·05 mg ($p < 0·05$). However, this dose of oestrogen is much higher than that commonly used in menopausal patients.

In our controlled study of conjugated oestrogen therapy in 30 patients[4] (Premarin 1·25 mg daily) blood pressure was measured at each monthly consultation. No significant changes in blood pressure occurred and there was no difference between patients taking oestrogen and those taking placebo. In our study of piperazine oestrone sulphate[5] (1·5 mg twice daily) in 55 patients, blood pressure was measured initially and at each two-monthly consultation for 14 months. No significant difference was observed between the groups. In fact, on both treatments there was a slight mean fall in blood pressure.

Our experience is that oestrogen therapy in the usual dosage does not cause a rise of blood pressure. It does, however, cause changes in coagulation,[4-7] and should therefore be used with caution in patients prone to thromboembolic disease.

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SIR,—In reply to the letters about our series "ABC of blood pressure reduction" (13 December, p 1635-6), we wish to make the following points.

We do not deny beta-blockers to insulin-dependent diabetics but advise caution in their use as hypoglycaemia occurs with beta-blockers[1] and there is an impaired metabolic response to it.[2 3] We agree with Dr Lilford's important point about the rate of rise of the blood pressure in pregnancy and the use of Albustix for the detection of proteinuria.

We are sorry to have confused Dr Keable-Elliott but there are no published large-scale trials of treatment of hypertension in the elderly and our views were based on personal experience rather than hard facts. The Framingham study[4] is not a trial of treatment and the Veterans Administration study[5] had only 30 patients in the 70-75 age group. Morgan *et al*[6] deal with a group of patients over the age of 50, which is hardly elderly by our criteria. The study of Priddle *et al*[7] showed that treatment reduced mortality but the two groups were not randomly allocated. We hope that the European Working Party on High Blood Pressure in the Elderly will be able to answer the question.

Our series was in the form of a follow-up to the "ABC of Blood Pressure Measurement" series of O'Brien and O'Malley. They strongly recommend[8] that phase 5 be used as the diastolic level. This is particularly important as all the recent large-scale trials of antihypertensive treatment use it.

Pfeffer[9] showed an association between oestrogen replacement use and hypertension.

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Postabortion sepsis and antibiotic prophylaxis

SIR,—Any technique which may reduce the potential morbidity associated with induced abortion warrants further investigation. However, the short report by Dr C Brewer (20 September, p 780) advocating the prophylactic use of antibiotics at abortion to prevent postabortion sepsis is incomplete and inconclusive. The methods used for termination in his study groups have not been stated, or the number of questionnaires returned by the patients for each group. Further, the diagnosis of pelvic infection was obviously uncertain in many of the stated cases (". . . cases that *seemed* to include pelvic infection . . .") and is surely too imprecise and unscientific a basis on which to advocate prophylactic treatment for the thousands of legal abortions performed in England and Wales each year.

A prospective follow-up study of patients who had undergone pregnancy termination managed in Oxford when prophylactic antibiotics had not been given has produced the "suspected infection" rates shown in the table. The method of post-conception prostaglandin-induced abortion and midtrimester prostaglandin abortion has previously been described[1 2] and follow-up data are available for 99% of the former and 90% of the latter, obtained at examination six weeks after abortion. For those patients whose pregnancy was terminated by vaginal aspiration under anaesthetic, follow-up was achieved by using completed questionnaires returned by patients. For this group only 64·5% returned a completed questionnaire; thus to obtain a more complete follow-up readmissions for suspected pelvic infection were detected by scrutiny of the emergency admission register at the Oxford gynaecological unit, the only admission

Pelvic infection associated with termination of pregnancy after no prophylactic antibiotics given

Abortion method:	Postconception prostaglandin	Vacuum aspiration	Intrauterine prostaglandins
Gestation (wk)	5–8	7–14	11–22
Total No	686	640	1860
Suspected pelvic infection: No (%)	7 (1·0)	11 (1·7)	27 (1·4)
Confirmed pelvic infection (laparoscopy or laparotomy): No (%)	1 (0·1)	—	1 (0·05)